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<p>The studies demonstrated that the injection of synapsin I, in addition to reducing the background spontaneous release of transmitter, produces a reduction of transmitter released by direct depolarization of the presynaptic terminal. Furthermore the spontaneous release mimics the time course of the reduction of the evoked release such that the two can be easily correlated. The effect of CaM kinase II injection produces an increased miniature frequency in parallel with the increase in evoked release without changing the time course of the miniatures. This indicated the probability of release was being enhanced both during spontaneous and evoked release, only increasing the likelihood of vesicular release. A similar type of calcium channel is also present for peptide secretion from the hypothalamus to the hypophysis.</p>				
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**Technical Report for AFOSR-89-0270**

R. Llinás/W. Berry

*"Synaptic Transmitter Release"*

February 1, 1990 - January 31, 1991

The research performed in the summer of 1990 related to three main areas. The first is the effects of synapsin I and CaM kinase II on miniature release in the squid giant synapse. This work studied the effect of dephosphorylated synapsin I on vesicular release as measured directly by the analysis of synaptic noise recorded in the postsynaptic axon. The results observed this summer were published in Proceedings of the National Academy of Science in a paper entitled "Effects of synapsin I and calcium/calmodulin-dependent protein kinase II on spontaneous neurotransmitter release in the squid giant synapse." The study demonstrated that the injection of synapsin I, in addition to reducing the background spontaneous release of transmitter, produces a reduction of transmitter released by direct depolarization of the presynaptic terminal. Furthermore the spontaneous release mimics the time course of the reduction of the evoked release such that the two can be easily correlated. The actual localization of the dephosphorylated synapsin I was directly monitored by imaging of the fluorescence produced by binding of a fluorophore onto the synapsin molecules.

The second aspect of the experiments was the injection of CaM kinase II, known to phosphorylate synapsin I and to increase transmitter release.

The effect of CaM kinase II injection produces an increased miniature frequency in parallel with the increase in evoked release without changing the time course of the miniatures. This indicated the probability of release was being enhanced both during spontaneous and evoked release, only increasing the likelihood of vesicular release.

The second aspect of research during the summer relates to peptidergic nerve terminal release in mammals using optical measurements. The methods, which consisted of determining light scattering produced by activation of a presynaptic terminal in the stalk of the hypophysis, were studied before and after the administration of FTX (funnel web spider toxin). This toxin, which is

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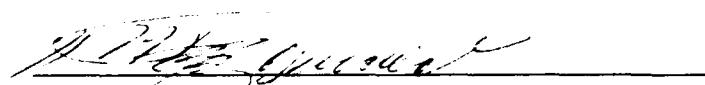
known to block transmission at the squid giant synapse, does so by a direct effect on voltage-dependent calcium channels in the presynaptic terminal. This set of experiments demonstrated that a similar type of calcium channel is also present for peptide secretion from the hypothalamus to the hypophysis. A short communication was published in collaboration with Salzberg, Kumar and Komuro.

A third set of experiments related to the effects of synapsin I on synaptic facilitation at the crayfish neuromuscular junction. Indeed while synapsin I has been shown to regulate the amount of transmitter release by action potentials, another study was performed to determine whether synapsin I is also capable of reducing or modulating facilitation of presynaptic release in crayfish neuromuscular junction. This junction is known to demonstrate facilitation, and thus synapsin was injected presynaptically. This study was done under direct observation of the preterminals using both Fura 2 to determine the level of calcium entry and fluorescent synapsin I to determine migration of presynaptically injected protein.

The results demonstrated that synapsin I facilitation is reduced beyond the level of reduction of the evoked transmitter release. This research is essential in understanding the mechanism for synaptic facilitation and the role of synapsin I in this mechanism.



Signature - Principal Investigator


Signature - Senior Director  
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